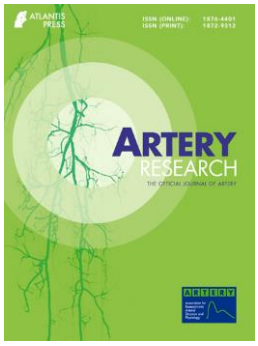

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1.3: CENTRAL PRESSURES AND WAVE REFLECTIONS ARE INDEPENDENTLY ASSOCIATED WITH MAJOR ADVERSE CARDIOVASCULAR EVENTS IN MEN WITH ERECTILE DYSFUNCTION

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1.1
DIABETES AND CENTRAL BLOOD PRESSURE IN CORONARY PATIENTS

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Background: Relative (represented by pulsatility) as well as absolute (pulse pressure) changes of central blood pressure (BP) were shown to predict cardiovascular (CV) complications in coronary patients. However, the influence of diabetes (a major CV risk factor) on the values of BP-derived indices is unknown.
Methods: The study group consisted of 1239 patients with coronary artery disease (988 men and 251 women mean age: 58.6±10.1 years) undergoing coronary angiography. Demographic and clinical information as well as cuff brachial and invasive ascending aortic BP during catheterization were obtained. Diabetes was defined as being treated for diabetes or having fasting glucose ≥ 7.0mmol/l. We defined pulsatility as the ratio of pulse pressure (PP) to mean BP and pulsatility index as the ratio of PP to diastolic BP. Multivariate regression analysis was used to assess the effect of diabetes on the values of BP-derived indices.
Results: Diabetes was present in 222 (17.9%) patients. Among them 84 (37.8%) were prescribed insulin, 96 (43.2%) oral drugs, and 42 (18.9%) only diet. β-blockers were prescribed to 82.4% vs 87.2% (p=NS), ACE-inhibitors/sartans to 75.2% vs 57.6% ($p<0.05$), Ca blockers to 21.2% vs 15.7% ($p<0.05$), diuretics to 41.0% vs 20.1% ($p<0.05$), for diabetics and non-diabetics respectively. The effect of diabetes on central pressure is presented in the table. Diabetes was not independently related to the value of peripheral BP-derived indices.
Conclusion: Diabetes is independently related to the higher values of central PP, pulsatility and pulsatility index. This may contribute to higher CV risk in diabetics.

Table 1

BP — related variables	The mean difference between diabetics and non-diabetics (95% CI)	
	Univariate	Multivariate*
Systolic blood pressure [mmHg]	4.37 (1.03 - 7.70)	2.28 (-1.22 - 5.78)
Diastolic blood pressure [mmHg]	-1.16 (-2.82 - 0.50)	-1.11 (-2.98 - 0.76)
Mean blood pressure [mmHg]	0.66 (-1.34 - 2.66)	0.01 (-2.22 - 2.23)
Pulse pressure [mmHg]	5.53 (2.89 - 8.17)	3.39 (0.80 - 5.99)
Pulsatility	0.05 (0.03 - 0.08)	0.03 (0.01 - 0.06)
Pulsatility index	0.09 (0.05 - 0.13)	0.06 (0.02 - 0.10)

* Age, sex, brachial systolic and diastolic BP, ejection fraction, extent of coronary atherosclerosis, NYHA class, heart rate, creatinine level, risk factors and treatment are included in the model.

1.2
HOW DOES OBESITY INFLUENCE ARTERIAL STIFFNESS IN ASYMPTOMATIC ADULTS?

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Central obesity is an important cause of cardiovascular disease. It's well-known that aortic pulse wave velocity (aoPWV) is a strong predictor of cardiovascular events. However the potential correlation between fat accumulation and increased arterial stiffness is poorly investigated. The aim of this study was to assess the association between obesity and aortic stiffness in normotensive adults.
Patients and methods: AoPWV was assessed in apparently healthy, asymptomatic patient population using an invasively validated oscillometric device (TensioMed Arteriograph). AoPWV-values were stratified according to their BMI-values into three categories: normal weight (BMI<25), overweight (BMI: 25-30) and obese (BMI>30). Data are reported as mean and SD for continuous variables. For data comparison, a Student's t-test was used with a significance level of 0.05. Statistical analysis was carried out with IBM SPSS 20 statistical software.
Results: 9076 normotensive individuals (3749 male — 41.3%, and 5327 female — 58.7%) without any antihypertensive, antidiabetic or antilipemic medication were included into the analysis with a mean age of 48.2±14.1 yrs. 4374 individuals were lean (48%), 3346 were overweight (37%) and 1353 were obese (15%) according to BMI-values. Mean aoPWV of lean subjects was significantly better than overweight or obese individuals (8.6±2.41 m/s, 9.3±2.43 m/s ill. 9.8±2.52 m/s respectively $p<0.05$).
Conclusions: This is the first population-based study to report the effect of weight on vascular stiffness measured by oscillometric method in adults with wide age range. Our results confirmed that overweight and obesity are major determinants of arterial stiffness. The revealed association suggests that weight gain begins to influence on the vascular system at a very early stage of vascular aging. Nevertheless the effect of weight loss on arterial function needs to be further investigated.

1.3
CENTRAL PRESSURES AND WAVE REFLECTIONS ARE INDEPENDENTLY ASSOCIATED WITH MAJOR ADVERSE CARDIOVASCULAR EVENTS IN MEN WITH ERECTILE DYSFUNCTION

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Purpose: Erectile dysfunction (ED) confers an independent risk for cardiovascular events and total mortality. Central pressures and wave reflection

indices independently predict cardiovascular events. Aim of this study is to investigate whether central haemodynamics predict major adverse cardiovascular events (MACEs) in ED patients beyond traditional risk factors.
Methods: MACEs in relation to aortic pressures and Augmentation index (AIx) were analyzed with proportional hazards models in 398 patients (mean age, 56 years) without established cardiovascular disease (CVD).
Results: During the mean follow-up period of 6.5 years, a total of 29 (6.5%) MACEs occurred. The adjusted relative risk (RR) of MACEs was 1.062 (95% CI 1.016—1.117) for a 10-mmHg increase of aortic systolic pressure, 1.117 (95% CI 1.038—1.153) for a 10-mmHg increase of aortic pulse pressure (PP), and 1.191 (95% CI 1.056—1.372) for a 10% absolute increase of AIx. The based on categories for 10-year coronary heart disease risk and adapted at 6.5 years overall net reclassification index (NRI) showed marginal and indicative risk reclassification for AIx (15.7%, P=0.12) and aortic PP (7.2%, P=0.20) respectively.
Conclusions: Our results show for the first time that higher central pressures and wave reflections indices are associated with increased risk for a MACE in patients with ED without known cardiovascular disease. Considering the adverse prognostic role of central haemodynamics on outcomes, the present findings may explain part of the increased cardiovascular risk associated with ED.

2.1
THE RELATIVE IMPORTANCE OF CENTRAL AND BRACHIAL BLOOD PRESSURE IN PREDICTING CARDIOVASCULAR EVENTS: AN INDIVIDUAL PARTICIPANT META-ANALYSIS OF PROSPECTIVE OBSERVATIONAL DATA FROM 22,433 SUBJECTS

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Systolic blood pressure (SBP) differs between the brachial artery and aorta. Prospective data suggest that central pressure predicts future cardiovascular events, but it is unclear if it is superior to brachial pressure.
Methods and Results: A systematic review and individual participant data meta-analysis from 15 studies was undertaken. Study-specific associations of central and brachial pressure with cardiovascular outcomes, with and without mutual adjustment, were determined using Cox proportional hazard models, and random effect models to estimate pooled estimates. Of 22,433 participants, 908 had a myocardial infarction (MI) and 641 a stroke. The pooled age, sex, height and heart rate adjusted hazard ratio (HR) [95% CI] per SD increase in brachial SBP was 1.17 [1.03, 1.32] for MI and 1.28 [1.13, 1.46] for stroke and 1.16 [1.02, 1.33] and 1.33 [1.15, 1.53] for central SBP, respectively. Mutual adjustment attenuated the HRs for MI: brachial SBP (1.16 [0.90, 1.48]), central SBP (1.09 [0.87, 1.38]) and stroke: brachial SBP (1.18 [0.97, 1.42]), central SBP (1.19 [0.99, 1.44]). However, associations between central SBP and stroke, after adjustment for brachial SBP, were higher in those aged <61 years than in older individuals (1.83 versus 1.08 p-interaction <0.001).
Conclusion: Brachial and central SBP have similar associations with future CV events. Larger studies are required to test whether central SBP may be a more powerful predictor of stroke risk in younger individuals.

2.2
CENTRAL-TO-PERIPHERAL DIASTOLIC BLOOD PRESSURE ATTENUATION IN HEALTHY ADOLESCENTS AND THE EFFECTS OF HEART RATE. THE MACISTE STUDY

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Background: Heart rate (HR) is directly associated to central-to-peripheral pulse wave amplification. We aimed at evaluating the associations between heart rate and each BP component in a cohort of healthy adolescents.
Objective: 470 healthy adolescents (17±1.4 years, 56% boys, brachial BP 123/67±11/7 mmHg, HR 72±12 bpm) were enrolled in the present study. Brachial BP was measured on 3 occasions by validated devices. Central BP was estimated by radial and brachial applanation tonometries, and calibrated to brachial MAP/DBP (SphygmoCor).
Results: Brachial and central BP were 123/67±11/7 mmHg and 105/69±9/8 mmHg. SBPamp was 1.17±0.04, PPamp was 1.57±0.13, while DBP amplification was 0.97±0.01 (DBP attenuation). HR had a direct correlation with brachial and central DBP (r=0.38 and r=0.46, both p<0.01) and central SBP (r=0.09, p=0.04), but not with peripheral SBP (p=0.59), and a negative one with brachial and central PP (r=-0.24 and r=-0.37, both p<0.01). HR had a positive association with PPamp (r=0.38, p<0.01), and a negative one with SBPamp (r=-0.14, p<0.01) and DBPamp (r=-0.55, p<0.01). The slope of BP change for each 10-bpm HR increase was steeper for central DBP (2.8±0.3 mmHg), than for peripheral DBP (2.2±0.3 mmHg, p for difference between regression coefficients <0.01), and for central and brachial DBP than for central SBP (0.7±0.3 mmHg, both p<0.01).
Conclusions: HR is associated with more pronounced changes in DBP than in SBP, and in central than peripheral DBP. Increasing HR may attenuate DBP from centre to periphery. The assumption that DBP is constant along the arterial tree may not be valid during dynamic conditions.

2.3
DETERMINANTS OF INAPPROPRIATELY HIGH PULSE WAVE VELOCITY IN HYPERTENSIVE PATIENTS: A RETROSPECTIVE CROSS-SECTIONAL COHORT STUDY

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Background: Age and blood pressure (BP) are known to be the main determinants of large artery stiffness. However other factors may lead to an inappropriately high pulse wave velocity (PWV). We investigated the determinants of inappropriately high PWV in hypertensive patients and their possible role in causing organ damage accrual.
Methods: Hypertensive patients were selected among those attending a visit in our Hypertension Outpatient Clinic and undergoing carotid-femoral PWV by applanation tonometry, and cardiac and carotid ultrasound during a 5-year period (2006-2011). Inappropriately high pulse wave velocity (PWV) was calculated as the ratio between the observed value and the values predicted according to the formula derived from international reference values stratified by age and mean BP (oPWV/pPWV)[1,2].
Results: 731 hypertensive patients were selected (age 30-88 years, 42% women, 57% taking BP-lowering drugs). Median oPWV/pPWV was 10±2% (range 6±1-19±6%). In a multiple linear regression model, independent determinants of oPWV/pPWV were: daylight hours (β -1.59, SE 0.33), age (β -0.65, SE 0.08), BMI (β 0.64, SE 0.20), blood glucose (β 0.19, SE 0.05), carotid atherosclerosis (β 2.48, SE 1.20). Though oPWV/pPWV was significantly higher in men and current smokers, the association disappeared in the